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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/651,305	08/28/2003	Chia-Gee Wang	U 014775-5	9020

140 7590 09/02/2008

LADAS & PARRY LLP
26 WEST 61ST STREET
NEW YORK, NY 10023

EXAMINER	
POLANSKY, GREGG	
ART UNIT	PAPER NUMBER
1611	
MAIL DATE	DELIVERY MODE
09/02/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/651,305	WANG, CHIA-GEE	
	Examiner	Art Unit	
	GREGG POLANSKY	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-99* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5,7,12,13,16-36,38,40,42,47,48,51-65,67,69,71,76-88,90,92 and 97-99* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 2,4,6,8-11,14,15,37,39,41,43-46,49,50,66,68,70,72-75,89,91 and 93-96.

DETAILED ACTION

Status of Claims

1. Applicant's response, filed 6/02/2008, to the Office Action mailed 11/29/2007 is acknowledged. Applicant amended Claims 1, 17, 19, 20, 22, 52, 54, 55, 57, 78-80, 82, and 87, and presented arguments in response to the Office Action.

2. Claims 1-99 are pending.

3. Claims 2, 4, 6, 8-11, 14, 15, 37, 39, 41, 43-46, 49, 50, 66, 68, 70, 72-75, 89, 91 and 93-96 remain withdrawn from consideration because they do not read on the elected species (cisplatin). 37 CFR 1.142(b)

4. Claim 1, 3, 5, 7, 12, 13, 16-36, 38, 40, 42, 47, 48, 51-65, 67, 69, 71, 76-88, 90, 92 and 97-99 are presently under consideration.

5. Applicant's arguments have been fully considered and are persuasive in part. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 2, 5, 7, 12, 13, 16-36, 38, 40, 42, 47, 48, 51-65, 67, 69, 71, and 76-84 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the Specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a New Matter rejection**.

Instant Claim 1 has been amended to recite a "method for **preferential disruption** of malfunctioning cells in a living mammal, which comprises…" (emphasis added). The Specification discloses a method of "treating" malfunctioning cells; it does not disclose a method for "preferential disruption" of malfunctioning cells. A method for the "preferential disruption" of malfunctioning cells is considered to be new matter.

8. Claims 1, 3, 5, 7, 12, 13, 16-36, 38, 40, 42, 47, 48, 51-65, 67, 69, 71, 76-88, 90, 92 and 97-99 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Claims 1 and 65 recite "line emission x-rays of an energy selected to cause emission of Auger electrons from said pre-selected element [Pt] of said compound [cisplatin] in a dose effective to disrupt DNA proximate to the irradiated pre-selected element". Claims 20, 22, 55, 57, 80, 82, and 85 recite "wherein the target and the e-beam energy are selected to provide monochromatic line emission x-rays having an

energy above and sufficiently near the K-absorption edge" (Claims 20, 55, 80, and 85), or "L-absorption edge" (Claim 22, 57, 82, and 85) "of the pre-selected element [Pt] of the compound [cisplatin] to cause said emission of Auger electrons" (emphasis added). The Specification does not disclose the energy of line emission x-rays required to cause emission of Auger electrons from the platinum in the elected compound, cisplatin. The Specification does not disclose the K-absorption edge or L-absorption edge for platinum. Additionally, the Specification does not disclose a target and e-beam energy combination necessary to provide monochromatic line emission x-rays having an energy above and substantially near the K-absorption or L-absorption edge of platinum. Therefore, the disclosed claims are rejected for failing to meet the written description requirement.

After further consideration, the Examiner amended the rejection of the previous Office Action by removing the passage stating "Claims 30-35 recite a method of treating malfunctioning cells which have been removed from a mammal and then returned to the mammal after said treatment. The Specification does not disclose any steps necessary to practice this method aside from a disclosure of the possibility of its use."

9. Applicant argues that the Examiner has "respectfully overlooked that the subject matter for which the Examiner contends there is a lack of adequate written description is described in the original claims. See original claims 1, 20, 22, 30-35, 55, 80, 82, 85, and 98".

The Examiner has reviewed the original claims and has amended the rejection by removing the passage stating "Claim 98 recites a "method according to claim 85,

wherein the pre-selected element of the compound has an atomic number in the range of from 35 to 83. The Specification discloses an atomic number range of 35 to 79, not a range of 35-83.".

Applicant argues that the "claims are commensurate in scope with the disclosure as filed and the only reasons presented by the Examiner to support the rejection pertain to limitations that are not claimed and that, in any event, were well known to those of skill in the art as of the application filing date (e.g., the K-absorption or L-absorption edge for platinum)."

This argument is not well taken. The limitations the rejection is based on are limitations quoted directly from the instant claims.

10. Claims 1, 3, 5, 7, 12, 13, 16-36, 38, 40, 42, 47, 48, 51-65, 67, 69, 71, 76-88, 90, 92 and 97-99 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in

the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

The instant specification fails to provide guidance that would allow the skilled artisan to practice that instant invention without resorting to undue experimentation in view of further discussion below.

The nature of the invention and the breadth of the claims:

The claimed invention relates to a method for the preferential disruption of malfunctioning cells, including tumors or cancer, in a living mammal, with comprises the steps of: (a) administering a compound (e.g., cisplatin) which associates with DNA in cells of said mammal, wherein said compound comprises a pre-selected element (e.g., platinum); and then (b) irradiating the select region in which malfunctioning cells, having said compound associated with DNA, are located, with line emission x-rays of an energy selected to cause emission of Auger electrons from said pre-selected element of said compound in a dose effective to cause disruption of DNA proximate to the irradiated pre-selected element.

The claims are very broad and inclusive to all types of tumors, cancers, polyps, pre-cancerous cells, and other malfunctioning cells.

The state of the prior art, relative skill of those in the art and the predictability of the art:

In just considering therapeutic treatments for cancers and tumors, the prior art teaches there is no one specific treatment that is effective for all types of cancer. See

Goldman et al., Ed., Cecil Textbook of Medicine, 21st Edition, Volume 1, 2000, Table 198-5, page 1065, Table 198-6, page 1066, Table 198-8, page 1068, and Table 198-9, page 1071. One of skill in the art would also expect that different cell types would have different affinities for the selected compound of the present invention, leading to variable responsiveness to the instant methods.

The relative skill of those in the art is that of a Ph.D. or M.D.

The present invention is unpredictable given the breadth of the claims.

The amount of direction or guidance provided and the presence or absence of working examples:

Applicant's specification does not disclose a method for the preferential disruption of malfunctioning cells. Further, Applicant's specification does not contain any working examples showing what types of malfunctioning cells were treated by the instant invention.

The quantity of experimentation necessary:

Since Applicant's specification fails to disclose a method for the preferential disruption of malfunctioning cells, experimentation is not possible. Further, Applicant has failed to provide guidance as to how the instant invention (including specific compounds and specific chemical elements used for the e-beam target) will treat all types of abnormal cells. Therefore, undue experimentation would be required to practice the invention as it is claimed in its current scope.

11. Applicant argues the Goldman et al reference relied upon "show the alleged unpredictability in using **chemotherapy** for treating all types of cancer cells, but has respectfully overlooked the fact that the claims are directed to **radiation therapy**.".

This argument is not well taken. Applicant is respectfully directed to instant Claim 1 (a) which recites "**administering a compound** which associates with DNA cells of said mammal…" (emphasis added).

Applicant argues "the claimed invention provides a tool for the preferential or selective removal of tumor cells…", and that the skilled artisan "would be able to determine without undue experimentation those tumors, if any, which may not be operable with the selected method".

This argument is not convincing. The full scope of the claims is drawn to the preferential disruption of malfunctioning cells. This would include any malfunctioning cells and is not limited to tumors. Even if the claims were limited to tumor cells, one of skill in the art would not expect that cisplatin (the elected compound) would necessarily associate with all types of tumor cells.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

14. Claims 1, 3, 5, 7, 12, 13, 16-36, 38, 40, 42, 47, 48, 51-65, 67, 69, 71, 76-88, 90, 92 and 97-99 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mills (U.S. Patent No. 6,224,848), in view of Wang (U.S. Patent No. 5,627,871).

Mills teaches *inter alia* a method for eliciting tissue necrosis, in treating *inter alia* cancer, by administering a compound (e.g., cisplatin) that binds to targeted tissue DNA, wherein said compound comprises an atom (e.g., platinum) that is excitable with radiation in a distinct narrow frequency band and energy level, causing an Auger electron cascade resulting in radiolysis of DNA. See Abstract and columns 108-110, claims 1, 5, and 9). Note that the compound, cis-diamminedichloroplatinum (II), taught by Mills in column 109, line 8, is the chemical name of cisplatin. Since cisplatin taught in the reference is the same as cisplatin recited by the instant invention, the properties of the elected compound (cisplatin) recited by the instant claims would also be encompassed by the cisplatin taught by Mills. For instance, the rate of physiological excretion of cisplatin and stability against dissociation of platinum from cisplatin during the time prior to complete excretion of cisplatin (e.g., instant Claims 16 and 17 respectively) would be identical in both the reference and the instant invention.

Similarly, the K- and L-absorption edge of platinum and the amount of Auger electrons released from the platinum in cisplatin would be identical in the Mills reference and the instant claims.

The instant invention differs from the cited reference in that the cited reference does not teach the Applicant's preferred method of eliciting Auger electron cascade (i.e., line emission x-rays) from the selected element (i.e., platinum). However, the secondary reference, Wang, teaches the preferred line emission x-rays to be well known in the art. See column 10, lines 27-51. Wang teaches an end window transmission x-ray tube possessing a metal foil target on said end window, the thickness and composition of the metal foil target and the e-beam energy focused thereupon generate a micro-focused bright line beam x-rays of pre-selected energy. See Abstract.

Therefore, one skilled the art would have understood that the substitution of one monochromatic x-ray source (with distinct and specific frequency and energy level properties) for another source (with the same energy properties) would produce and achieve the same results (causing a Auger electron cascade from the platinum in the cisplatin) in the absence of evidence to the contrary. It would have been obvious to the artisan to use the x-ray source taught by Wang because of the increased convenience and logistics of using the smaller and more easily transported x-ray tube as opposed to the synchrotron taught by Mills.

The references do not teach the treatment of cells removed from and returned/transplanted back to a mammal. The references do not teach a kit comprising

an x-ray tube having a target comprising a selected metal, and a compound (cisplatin) comprising a selected element (Pt).

On skilled in the art would have well versed in the practice of removing bone marrow and various other cells from the body for treating certain cancers (e.g., x-ray treatment) and returning/transplanting these cell back into the body. It would have been obvious to use the methods taught by Mills and modified by the teachings of Wang to seek an improved cancer therapy. It would also have been obvious to said artisan to "package" the essential components necessary to practice these methods. One would have been motivated to do so to provide a more convenient and efficient means for practicing a method of cancer therapeutics.

15. Applicant argues the reference to Millis teaches away from radiation therapy with the use of x-rays and thus "there would have been no rationale or reason to modify Mills with Wang, as proposed by the Examiner".

This argument is not convincing. As presented *supra*, one skilled the art would have understood that the substitution of one monochromatic x-ray source (with distinct and specific frequency and energy level properties) for another source (with the same energy properties) would produce and achieve the same results (causing a Auger electron cascade from the platinum in the cisplatin) in the absence of evidence to the contrary. It would have been obvious to the artisan to use the x-ray source taught by Wang because of the increased convenience and logistics of using the smaller and more easily transported x-ray tube as opposed to the synchrotron taught by Mills.

Further, Applicant is directed to M.P.E.P. 2123 II. Nonpreferred And Alternative Embodiments Constitute Prior Art which states:

> Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. *In re Susi*, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). "A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." *In re Gurley*, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994) (The invention was directed to an epoxy impregnated fiber-reinforced printed circuit material. The applied prior art reference taught a printed circuit material similar to that of the claims but impregnated with polyester-imide resin instead of epoxy. The reference, however, disclosed that epoxy was known for this use, but that epoxy impregnated circuit boards have "relatively acceptable dimensional stability" and "some degree of flexibility," but are inferior to circuit boards impregnated with polyester-imide resins. The court upheld the rejection concluding that applicant's argument that the reference teaches away from using epoxy was insufficient to overcome the rejection since "Gurley asserted no discovery beyond what was known in the art." 27 F.3d at 554, 31 USPQ2d at 1132.).

Conclusion

16. Claims 1, 3, 5, 7, 12, 13, 16-36, 38, 40, 42, 47, 48, 51-65, 67, 69, 71, 76-88, 90, 92 and 97-99 are rejected.

17. No claims are allowed.

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GREGG POLANSKY whose telephone number is (571)272-9070. The examiner can normally be reached on Mon-Thur 9:30 A.M. - 7:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila G. Landau can be reached on (571) 272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gregg Polansky/
Examiner, Art Unit 1611

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614